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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/24/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/500,635	Applicant(s) LEON ET AL.	
	Examin r Michael Wilson	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1632.

Claims 1-20 have been canceled. Claims 21-32 have been added and are under consideration in the instant application.

Applicant's arguments filed 2-19-02, paper number 12, have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

1. The first line of the specification needs updated.

Claim Objections

2. Claims 21-32 are objected to because of the following informalities:

a. The phrase "Primavril gum" (claim 21) should be --primordial germ--.

b. The word "genes" in claim 24, line 2, should be --genus--.

c. The word "turney" in claim 31 should be --turkey--.

d. The word "heterologus" in claim 32 should be --heterologous--.

Appropriate correction is required. Please check the spelling in future amendments.

Claim Rejections - 35 USC § 112

3. New claims 21-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrases "embryonic germ (EG) cells", "compact multilayer like appearance", and "in the absence of feeder cells" as newly recited in claim 21 do not have support in the specification as originally filed.

Culturing PGCs in bFGF, SCF, LIF and IGF in the absence of feeder cells (claim 21) does not have support in the specification as originally filed.

Culturing PGCs in bFGF, SCF, LIF and IGF in the absence of feeder cells and sustaining the culture for 14 days, 28 days or 4 months (claims 26-28) does not have support in the specification as originally filed.

Culturing PGCs for 28 days does not have support in the specification as originally filed.

The phrase "heterolus DNA system" does not have support in the specification as originally filed.

As such, these phrases are new matter. Applicants are requested to provide support for these limitations by page and line number.

4. New claims 21-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for culturing avian PGCs in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells, does not reasonably provide enablement for one of skill to determine the conditions essential to maintain cells for 14 days, 28 days or 4 months, the conditions essential to produce a culture having a "compact multilayer like appearance," using cells transfected with DNA to make transgenic avians in which exogenous protein is isolated or in which the phenotype of the avian is altered by the DNA, or obtaining EG cells from avian species other than chickens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 21 requires culturing avian PGCs in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells wherein LIF, bFGF, SCF and IGF are present in amounts sufficient to maintain the PGCs for a prolonged period of time, e.g. 14 days, 28 days or 4 months. The specification describes "long term cell culture medium" (pg 21, line 3 through pg 22, line 14), but this section of the specification does not teach the "long term cell culture medium" was used in the absence of feeder cells. While the specification states feeder cells did not improve "long term culture" of the PGCs (pg 27, line 14), the specification does not teach PGCs were maintained in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells for a 14 days, 28 days or 4 months. The specification describes maintaining PGCs for 7 days (pg 22, line 4) and PGC clumps for up to four weeks (pg 22, line 7); however, the specification does not teach this was

done in the absence of feeder cells. Overall, the specification does not describe the essential conditions required to maintain PGCs for 14 days, 28 days, or 4 months in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells.

Claim 21 requires culturing avian PGCs in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells, wherein a culture comprising PGCs and EG cells is obtained. The specification teaches transplanting PGCs into chicken embryos such that germ and somatic cell chimeras that were not somatic cell chimeras were obtained (pg 25, lines 6-19). While the specification teaches culturing PGCs in bFGF, IGF, SCF and LIF (page 21, lines 4 and 17), and states feeder cells did not improve "long term culture" of the PGCs (pg 27, line 14), the specification does not teach obtaining EG cells (which provide germ and somatic cell chimeras) by culturing PGCs in the presence of LIF, bFGF, SCF and IGF and the absence of feeder cells. As such the specification does not describe the essential conditions required to maintain PGCs in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells such that EG cells are obtained as claimed.

Claim 21 requires culturing avian PGCs in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells wherein a culture having a compact multilayer like appearance is obtained. The specification does not teach a culture having this description. The specification does not teach the conditions that are essential to obtain a culture having this description. The specification does not teach the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells are essential to obtain a culture having this description. As such the specification does not

describe the essential conditions required to obtain a culture having a compact multilayer like appearance using PGCs maintained in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells.

Claim 29 is directed toward a method of culturing avian PGCs for prolonged periods and transfecting the PGCs/EG cells produced with a nucleic acid sequence. Claim 32 is directed toward a culture of PGCs and EG cells wherein the PGCs are transfected with DNA. The only disclosed purpose for transfecting PGCs or EG cells is to make a transgenic avian which is used to isolate exogenous proteins from the avian (page 8, line 22) or to change the phenotype of the bird (page 2, line 21). The claims are rejected for reasons of record because the specification and the art at the time of filing did not teach how to use transfected avian PGCs/EG cells to make transgenic avians in which exogenous protein is isolated or in which the phenotype of the avian is altered.

The specification does not enable obtaining any avian EG cells as broadly claimed. The state of the art at the time of filing was such that EG cells had only been obtained in chickens and mice. An EG cell is considered a cell capable of becoming both a somatic and germ cell upon being introduced into an embryo and is equivalent to an ES cell. Wagner (May 1995, Clin. and Experimental Hypertension, Vol. 17, pages 593-605) and Mullins (1996, J. Clin. Invest., Vol. 98, pages S37-S40) taught obtaining ES cells from species other than mice is unreliable. Simkiss (1990, 4th World Congr. Genetic Appl. Livestock Prod., Vol. 16, pg 111-114) and Petitte (1990, Development, Vol. 108, pg 185-195) taught chicken PGCs capable of producing somatic and

germ cell chimeric chickens - these PGCs are equivalent to EG cells. As seen in the art cited above, the stage of isolation, cell morphology and culture conditions required for chicken and mouse ES cells differ. The specification does not correlate the parameters required to obtain chicken ES cells with those required to obtain ES cells from other avian species. Given the teachings in the art taken with the teachings in the specification, the parameters required to obtain EG cells in non-chicken avians were not within the realm of routine experimentation for one of skill in the art at the time the invention was made.

The specification does not enable using cells transfected with DNA to make transgenic avians in which exogenous protein is isolated or in which the phenotype of the avian is altered by the DNA. The only disclosed use in the specification for cells transfected with DNA is to make transgenics in which exogenous protein is isolated or in which the phenotype of the avian is altered by the DNA. The state of the art at the time of filing was such that the phenotype of transgenic avians with an exogenous transgene was unpredictable. Wall (1996, Theriogenology, Vol. 45, pages 57-68) discloses the unpredictability of transgene behavior due to factors such as position effect and unidentified control elements resulting in a lack of transgene expression or variable expression (paragraph bridging pages 61-62). Thus, the level and the specificity of expression of a transgene is greatly dependent on the specific transgene construct used making the phenotype of transgenic animals unpredictable. The specification teaches that stably transfected PGCs have not been obtained (page 30, line 8). Neither the specification nor the art teach obtaining stably transfected PGCs or making transgenic birds using transfected PGCs. Therefore,

the specification does not enable one of skill to use the method of transfecting PGCs or the transfected PGCs for the sole disclosed use of making transgenic avians because the specification does not enable changing the phenotype of the birds using transfected PGCs. Given the teachings in the specification taken with what was known in the art, it would have required one of skill undue experimentation to determine how to use cells transfected with a nucleic acid sequence as claimed (29, 32).

Applicants argue Vick (1993, Proceedings of the Royal Society of London, Vol. 251, No. 1332, pages 179-182) supports obtaining transgenic or chimeric avians. Therefore, applicants argue Vick enables transfecting PGCs/EG cells. Applicants argument is not persuasive because Vick does not support using transfected PGCs/EG cells to make transgenic avians in which exogenous protein is isolated or in which the phenotype of the avian is altered. Vick taught making transgenic chickens using PGCs infected with retrovirus. Vick did not teach the retrovirus was maintained in the offspring, the chickens expressed exogenous protein, the exogenous protein was isolated from the chickens, or the DNA caused a non-wild type phenotype in the chickens. This is consistent to the specification which teaches that stably transfected PGCs have not been obtained (page 30, line 8). Neither the specification nor the art teach using transfected PGCs/EG cells to make transgenic avians in which exogenous protein is isolated or in which the phenotype of the avian is altered by the DNA.

5. Claims 21-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants argue the cancellation of the claims in view of the pending claims overcome the indefiniteness rejections. Applicants argument is not persuasive.

Claim 21 is indefinite for reasons of record. The phrase "prolonged period of time" is not defined in the specification and does not have an art established definition such that the metes and bounds of the time period could be determined.

As newly amended, the phrase "containing essentially" in claim 21 is indefinite. The essential growth factors required to maintain PGCs for "prolonged periods of time" are not disclosed in the specification and are not readily apparent. In particular, it is especially unclear what growth factors applicants consider essential to maintain PGCs in culture for 14 days, 28 days or 4 months. It is unclear whether the conditions required to maintain the PGCs for 14 days is the same as those required to maintain PGCs for 28 days or for 4 months. It cannot be determined if IL-11 or ARMA are encompassed by the claims because it is unclear when or if IL-11 or ARMA are essential to maintain PGCs for "prolonged periods of time", 14 days, 28 days or 4 months.

Claim 21 is indefinite because the preamble is not commensurate in scope with the body of the claim. The preamble requires producing PGCs while the body of the claim results in a culture comprising PGCs and EG cells.

The phrase "said minimal amounts" (claim 22, 23) lacks antecedent basis. The range of amounts of the growth factors in claim 21 cannot be determined.

The metes and bounds of what applicants considered "desired" nucleic acid sequences (claim 29) cannot be determined. The "desired" nucleic acids are not described in the specification and have various boundaries in the art.

The phrase "which comprises said growth factors" (claim 30) does not further limit the claim. It does not further describe the method of claim 21 and does not describe the culture in claim 30.

Claim 32 is indefinite because it is unclear if the PGCs and EG cells are transfected or if only the PGCs with in the culture of PGCs and EG cells are transfected.

Claim 32 is indefinite because the term "heterologous" is unclear. The term "heterologous" is a relative term. It cannot be determined if it is being used in reference to the cell or the species. For example, is transfecting chicken cells with chicken DNA that is already present in the cell encompassed by the claim?

Claim 32 is indefinite because "system" is unclear. The metes and bounds of what applicants consider a DNA system cannot be determined.

Claim Rejections - 35 USC § 102

6. Claims 21-28, 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Pain (7-25-96, Development, Vol. 122, pages 2339-2348, UnCover online at

http://uncweb.carl.org/uncover/unchome.html) or in the alternative under 102 (a) as being anticipated by Pain (Pain et al., Aug. 1996, Development, Vol. 122, pages 2339-2348) and supported by Simkiss (Simkiss, 1994, MacLean, ed., Animals with novel genes, Transgenic birds, Cambridge Univ. Press, Cambridge England, NY, NY, pages 106-137) for reasons of record.

Pain taught culturing PGCs in complete media comprising bFGF, IGF, SCF and LIF in the absence feeder cells for 5 days (pg 2342, Fig. 2D). The patent office does not have the ability to determine how long the cells would grow under these conditions; therefore, without evidence to the contrary, these conditions are inherently capable of maintaining the PGCs for 4 months as claimed. Pain taught injecting cells into stage X embryos such that germline and somatic cell chimeras were obtained which indicates the culture had PGCs and EG cells as claimed (page 2340, col. 1, line 9; page 2340, col. 1, 4th and 5th full paragraphs).

Applicants argue Pain does not use "complete media". Applicants argument is not persuasive. The media taught by Pain is "complete" because it has "feotal bovine serum" (pg 2339, last line), it is described as "complete medium" (pg 2340, line 9), and it contains LIF, bFGF, SCF and IGF. The specification does not teach calf serum or glutamine are essential or required to make "complete" medium. Therefore, the claim does not exclude using media that does not have glutamine or calf serum. Furthermore, feotal bovine serum is equivalent to calf serum. Finally, it is not clear that glutamine is absent in the media because the base media, may have glutamine (pg 2339, 2nd to last line).

Applicants argue Pain teaches ARMA is "essential" to the media; therefore, Pain does not anticipate the claims. Applicants argument is not persuasive because pg 2342, col. 2, 1st para. merely teaches using ARMA in the media. It does not state ARMA is essential. Furthermore, the claims do not exclude media containing ARMA because it is unclear what is "essential" to maintain PGCs for prolonged periods in tissue culture as claimed (see 112/2nd).

Applicants argue pg 2340, col. 1, of Pain does not support long term culture of cells in the absence of a feeder layer. Applicants argue this is a general methodology section that does not discuss subsequent experiments or that the cells were cultured in both the absence of feeder cells and in the presence of the recited growth factors. Applicants argument is not persuasive because page 2340, col. 1, para. 5, last sentence, clearly teaches culturing PGCs in the absence of feeder cells.

Applicants argue pg 2342, Fig. 2B, does not correlate to the claims as newly written because the conditions did not require bFGF, IGF, SCF and LIF. However, Fig. 2D (see caption) states cells were cultured for 5 days in the absence of feeder cells and the presence of complete medium which has the recited growth factors (see pg 2340, col. 1, line 9). The conditions used in Fig. 2D are absent feeder cells because gelatin-coated dishes were used which is the alternative to feeder cells (pg 2340, col. 1, para. 5, last sentence).

Applicants argue the claims exclude using IL-11 which is taught by Pain. The claims do not exclude using IL-11 because it is unclear what is "essential" to culture avian PGCs for a

prolonged period of time as claimed (see 112/2nd). Nor does Pain require using IL-11 to maintain PGCs for a "prolonged period of time".

Overall, Pain taught culturing PGCs in complete media consisting essentially of LIF, bFGF, SCF and IGF and the absence of feeder cells as claimed. Pain taught these conditions were sufficient to maintain the PGCs for at least 5 days. While pg 2345, col. 2, teaches culturing PGCs for more than 160 days using LIF, bFGF, SCF, IGF, IL-11 and ARMA and feeder cells, Pain does not teach IL-11, ARMA or feeder cells are essential to do so.

Claims 30 and 31, directed toward a culture made by the method described above, are anticipated by Pain. The culture described by Pain does not differ from the culture claimed. The culture of Pain has a combination of PGCs and EG cells as claimed. The method used to make the culture as claimed does not alter the structure or function of the culture so as to distinguish it from the culture of Pain. The method does not bear patentable weight in considering the art for claims 30 and 31 because it does not alter the structure or function of the culture.

Therefore, Pain anticipates the claims.

Applicants arguments regarding a 103 are moot. The claims are not rejected under 103. Simkiss was cited in the 102 rejection to support the examiner's inherency argument that PGCs are present in the culture taught by Pain. Simkiss was not cited as a basis of the 102 rejection.

Double Patenting

7. Claims 21-26, 30 and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 of U.S. Patent No. 6,156,569, Dec. 5, 2000. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5 and 10-12 of '569 are obvious species of claims 21-28, 30 and 31 in the instant application. Claims 1-5 and 10-12 of '569 are directed toward a "pure population" of avian PGCs while the instant claims encompass any avian PGCs. The limitation of culturing the PGCs for at least 14 days in claim 1 of '569 is equivalent to claim 26 in the instant application. Applicants willingness to provide a terminal disclaimer upon allowance is acknowledged.

8. Claims 21-28, 30 and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 of U.S. Patent No. 6,156,569, Dec. 5, 2000 in view of Pain (Pain et al., 1996, Development, Vol. 122, pages 2239-2348). The claims of '569 are directed toward culturing pure PGCs for at least 14 days. The claims do not recite the limitations of maintaining the cells for at least 25 days or 4 months. However, Pain taught culturing avian embryonic cells for at least 160 days (page 2345, col. 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the claimed invention in '569 to maintain the PGCs for at least 25 days or 4 months. One of ordinary skill would have been motivated to maintain the PGCs for at least 25

increase the availability of the PGCs. Applicants willingness to provide a terminal disclaimer upon allowance is acknowledged.

Claims 29 and 32 appear to be free of the prior art of record because the prior art of record did not teach or suggest culturing avian PGCs in a culture medium comprising growth factors in amounts sufficient to maintain said PGCs for a prolonged period of time and transfecting the PGCs with a nucleic acid sequence.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

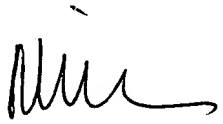
Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson



MICHAEL C. WILSON
PATENT EXAMINER